Remarks

Reconsideration of this Application is respectfully requested.

Upon entry of the foregoing amendment, claims 1-30 are pending in the application, with claims 1 and 2 being the independent claims. Claims 31-34, directed to non-elected subject matter, are sought to be cancelled without prejudice to or disclaimer of the subject matter therein. These changes are believed to introduce no new matter, and their entry is respectfully requested.

Based on the above amendment and the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding objections and rejections and that they be withdrawn.

I. Drawings

The drawings were objected to by the draftsperson under 37 C.F.R. § 1.84 or 1.152. *See* Paper No. 15, page 2. Applicants thank the Examiner for noting that correction of the defects can be deferred until the application is allowed.

II. Election/Restriction

The Examiner noted that claims 31-34 are drawn to an invention non-elected without traverse in Paper No. 7. *See* Paper No. 15, page 2. Accordingly, Applicants have cancelled claims 31-34 without prejudice to or disclaimer of the subject matter included therein.

III. Double Patenting

Claims 1-30 were rejected under the judicially-created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 1-16 of U.S. Patent No. 5,972,634. *See* Paper No. 15, pages 2-3. Applicants respectfully request that this rejection be held in abeyance until the remaining issues in the application have been resolved.

IV. Claim Rejections Under 35 U.S.C. § 112, First Paragraph

Claims 5-16 were rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. *See* Paper No. 15, page 4. Applicants respectfully traverse this rejection.

Applicants have previously submitted a Declaration under 37 C.F.R. § 1.132 by Professor Richard Strugnell (hereinafter, the "Strugnell Declaration") which states that one of ordinary skill in the art could have readily generated specific polyclonal antibodies to each of $A\beta_{1-42}$ and $A\beta_{1-40}$ with only routine experimentation. *See also* Amendment and Reply filed on October 3, 2001, pages 6-10.

The apparent basis for maintaining this rejection, however, is the Examiner's belief that *immunogens* for producing polyclonal antibodies specific to $A\beta_{1-42}$ and that do not cross react with $A\beta_{1-40}$, and vice versa, are not described in the specification. *See* Paper No. 15, page 5. The Examiner stated that:

> [f]rom Applicants declaration, it is clear that extensive experimentation must be performed to identify the appropriate immunogen that might possibly produce a

polyclonal antibody with the claimed binding specificity. Declarant proposes that all the information for the production of polyclonal antibodies with the requisite binding specificity is in the art. The examiner disagrees, the immunogen to produce the polyclonal antibody is the criticality upon which the production of the polyclonal antibody having the specifically claimed binding properties is based. This specific immunogen is not known to the art with respect to the production of polyclonal antibodies and is not taught by applicants.

Paper No. 15, page 7. Applicants respectfully disagree.

Applicants emphasize that identifying the appropriate immunogen(s) and using them to generate $A\beta_{1-40}$- and $A\beta_{1-42}$-specific polyclonal antibodies would have involved only routine experimentation in the art. The starting materials for obtaining the immunogen(s) for use in preparing the specific polyclonal antibodies of the invention were well known in the art at the time of the application. For instance, $A\beta_{1-40}$ and $A\beta_{1-42}$, as well as their sequences, were widely known. In addition, as noted in the Strugnell Declaration, "[a]s the two sequences differed only by two amino acid residues at the carboxyl terminus, a person of ordinary skill in the art would have known that it would be the carboxy end of these molecules that would bear the respective unique epitopes." *See* the Strugnell Declaration, paragraph 12.

The Strugnell Declaration further outlines an exemplary screening method that could have been used to identify the relevant immunogens. Specifically, the Strugnell Declaration discusses the method known as "Pepscan." *See* the Strugnell Declaration, paragraph 13. Using the Pepscan technique in conjunction with known amyloid β-specific monoclonal antibodies (*e.g.*, those described by Iwastsubo *et al.*, *Neuron 13*:45-53 (1994)), multiple peptides could have been screened for those that were recognized by $A\beta_{1-40}$-specific

antibodies but not by $A\beta_{1-42}$-specific antibodies, and vice versa. The identified peptides could have then been used to generate specific polyclonal antibodies. *See* the Strugnell Declaration, paragraph 14.

In response to Applicants' assertion that the relevant immunogens could have been easily obtained using routine methods in the art, the Examiner stated: "[t]hese arguments as set forth by Declarant's are not persuasive because the written description of the specification must enable one skilled in the art to make and use the reagents as required by the method and this fundamental requirement of 112, first paragraph, [that] can not be overcome by asserting that the skill in the art enables one to make such." *See* Paper No. 15, page 8.

Applicants respectfully remind the Examiner that an applicant is not limited to the confines of the specification to provide the necessary information to enable an invention. *See In re Howarth*, 654 F.2d 103, 105-6, 210 USPQ 689, 692 (CCPA 1981). An applicant need not supply information that is well known in the art. *See Genentech, Inc. v. Novo Nordisk*, 108 F.3d 1361, 1366, 42 USPQ2d 1001, 1005 (Fed. Cir. 1997); *Howarth*, 654 F.2d at 105-6, 210 USPQ at 692; *see also In re Brebner*, 455 F.2d 1402, 173 USPQ 169 (CCPA 1972) (finding a disclosure enabling because the procedure for making the starting material, although not disclosed, would have been known to one of ordinary skill in the art as evidenced by a Canadian patent). "'That which is common and well known is as if it were written out in the patent and delineated in the drawings.'" *Howarth*, 654 F.2d at 106, 210 USPQ at 692 (quoting *Webster Loom Co. v. Higgins* et al., 105 U.S. (15 Otto.) 580, 586 (1881)). Moreover, one of ordinary skill in the art is deemed to know not only what is considered well known in the art but also where to search for any needed starting materials.

Id. Since one of ordinary skill in the art could have easily obtained the immunogen(s) needed to generate polyclonal antibodies with the requisite specificities, as demonstrated by the Strugnell Declaration, it must be concluded that the enablement requirement of 35 U.S.C. § 112, first paragraph, is fully satisfied for claims 5-16.

Finally, Applicants respectfully assert that a *prima facie* case of non-enablement has not been established. In order to establish a *prima facie* case of lack of enablement, the Examiner has the initial burden to set forth a reasonable basis to question the enablement provided for the claimed invention. *See In re Wright*, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993). To satisfy this burden, "it is incumbent upon the Patent Office . . . to explain *why* it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement." *See In re Marzocchi*, 439 F.2d 220, 224, 169 USPQ 367, 370 (CCPA 1971) (emphasis in original).

Here, the Examiner has not provided any evidence or scientific reasoning that would indicate that producing the polyclonal antibodies used with and included within the present invention would have required undue experimentation. For instance, the Examiner has not provided a sufficient explanation as to why the exemplary method for screening peptides to identify those that could be used to generate $A\beta_{1-40}$- and $A\beta_{1-42}$-specific polyclonal antibodies, as disclosed in the Strugnell Declaration at paragraphs 13-18, would have involved undue experimentation or why it would have not been effective. The Examiner simply stated that "it is clear that extensive experimentation must be performed to identify the appropriate immunogen. . ." *See* Paper No. 15, page 7. Applicants respectfully assert

that such a conclusory statement is insufficient to establish a *prima facie* case of non-enablement.

The Examiner has also previously cited Campbell *et al.* for the proposition that the production of polyclonal serum is variable and not readily reproducible. *See* Paper No. 8, page 5. Campbell *et al.*, however, do not indicate that the production of polyclonal antibodies that can distinguish one molecule from another related molecule would require undue experimentation. Campbell *et al.* merely note certain technical issues that a skilled artisan may need to address in the process of preparing polyclonal antibodies generally. Since Campbell *et al.* do not specifically address the issue of producing polyclonal antibodies that can distinguish related molecules from one another, this document does not support a *prima facie* case of non-enablement.

In summary, Applicants submit that it would have required no more than routine experimentation for one of ordinary skill in the art to obtain one or more immunogens that, in turn, could have been used to generate $A\beta_{1-40}$- and $A\beta_{1-42}$-specific polyclonal antibodies. Moreover, the Examiner has not presented any specific evidence that would suggest that obtaining such immunogens and antibodies would have involved undue experimentation, and thus has failed to meet the PTO's burden of establishing a *prima facie* case of non-enablement. Accordingly, Applicants respectfully request that the rejection of claims 5-16 under 35 U.S.C. § 112, first paragraph, be reconsidered and withdrawn.

Conclusion

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Supplemental Amendment and Reply is respectfully requested.

Respectfully submitted,

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Version with markings to show changes made

Claims 31-34 are sought to be cancelled.